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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,424	04/13/2001	Stuart L. Schreiber	331D USD1	5917

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EXAMINER	
LOEB, BRONWEN	
ART UNIT	PAPER NUMBER
1636	9

DATE MAILED: 10/01/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/834,424	SCHREIBER ET AL.	
	Examiner	Art Unit	
	Bronwen M. Loeb	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *31 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 May 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: Copy of Papers Originally Filed information.

09/834,424

The following papers have not been made part of the permanent records of the United States Patent and Trademark Office (Office) for this application (37 CFR 1.52(a)) because of damage from the United States Postal Service irradiation process:

Mailroom Stamp Date	Certificate of Mailing Date
31 May 2002	10 May 2002 Paper # 7

The above-identified papers, however, were not so damaged as to preclude the USPTO from making a legible copy of such papers. Therefore, the Office has made a copy of these papers, substituted them for the originals in the file, and stamped that copy:

COPY OF PAPERS
ORIGINALLY FILED

If applicant wants to review the accuracy of the Office's copy of such papers, applicant may either inspect the application (37 CFR 1.14(d)) or may request a copy of the Office's records of such papers (*i.e.*, a copy of the copy made by the Office) from the Office of Public Records for the fee specified in 37 CFR 1.19(b)(4). Please do **not** call the Technology Center's Customer Service Center to inquiry about the completeness or accuracy of Office's copy of the above-identified papers, as the Technology Center's Customer Service Center will **not** be able to provide this service.

If applicant does not consider the Office's copy of such papers to be accurate, applicant must provide a copy of the above-identified papers (except for any U.S. or foreign patent documents submitted with the above-identified papers) with a statement that such copy is a complete and accurate copy of the originally submitted documents. If applicant provides such a copy of the above-identified papers and statement within **THREE MONTHS** of the mail date of this Office action, the Office will add the original mailroom date and use the copy provided by applicant as the permanent Office record of the above-identified papers in place of the copy made by the Office. Otherwise, the Office's copy will be used as the permanent Office record of the above-identified papers (*i.e.*, the Office will use the copy of the above-identified papers made by the Office for examination and all other purposes). This three-month period is not extendable.

Part of Paper No. 9

DETAILED ACTION

This action is in response to the amendments filed 14 April 2002 and 31 May 2002 in which the specification was amended and substitute drawings were filed.

Claims 1-7 are pending.

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The filing date for application 08/196,043 is incorrectly listed as February 11, 1994. According to USPTO records and the 08/196,043 file, that application was accorded a filing date of February 14, 1994.

Drawings

2. The corrected or substitute drawings were received on 31 May 2002. These drawings are acceptable.

Specification

3. The disclosure is objected to because of the following informalities: on pages 24 and 25, there are numerous small and difficult to read drawings of compounds.

Appropriate correction is required.

Claim Objections

4. Claim 4 is objected to because of the following informalities: It recites abbreviations (EPO, G-CSF, TPO, GH, IL-2) which are not defined at their first use in the claim set. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C.§112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-7 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is based on the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. §112, first paragraph "Written Description" Requirement published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claim 1 is drawn to a method for preparing an agent comprising covalently linking a first compound that binds to a protein mediator and a second compound that binds to another protein mediator such that binding of the agent effects a biological event. This is a genus claim in terms of any compound that binds to either protein mediator. The specification mentions FK506, cyclosporin, rapamycin, natural ligands of

various receptors, antibodies and any other compound that is known or found to bind to a receptor. This disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all the compounds that may be found to bind to a recepto,r based on the teachings in the specification. There is no discussion as to what structural feature(s) of compounds that bind to any particular receptor are, for any of the receptors of interest. While the specification teaches methods to screen or assay for such compounds, there is no structure-function teaching for any known ligands of the disclosed protein mediators that would indicate possession of a representative number of species of the vast genus of compounds encompassed by the claims. It is noted that a biomolecule described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the biomolecule, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed biomolecule. Therefore, the specification does not describe the claimed compounds that bind to protein mediators in such full, clear, concise and exact terms so as to indicate that Applicant has possession of these compounds at the time of filing the present application. Thus, the written description requirement has not been satisfied.

7. The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-7 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in reciting the phrases "capable of effecting" and "capable of binding". These phrases denote a latent ability which may or may not be observed in the invention. Amending the claim to recite "that effects" or "that binds" as appropriate will overcome this rejection.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

10. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Rodbard et al (USP 4,468,383). Rodbard et al teach making a dimeric analogue of enkephalin polypeptide monomers which binds to two δ opiate receptors and activates them thus effecting biological events. See entire document.

11. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Willey et al (Diabetologia (1978) 15:281, Abstract #377). Willey et al teach making a dimeric version of insulin monomers which upon binding to insulin receptors effect biological events including lipogenesis, anti-lipolysis hypoglycaemic effects. See entire abstract.

12. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Feuilloley et al (J. Steroid Biochem. (1990) 35:583-592). Feuilloley et al teach making covalently-linked dimers of ACTH fragments (specifically $(1\text{-}24)_2$Lys) which, when bound to their cognate membrane receptor, cause stimulation of corticosterone and aldosterone release. See entire document, especially Table 1, p. 585-586 "Effect of ACTH(1-24) and dimeric ACTH$(1\text{-}24)_2$Lys on corticosteroid secretion" and Fig. 2b.

13. Claims 1, 2, 5 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Engel et al (Biochemistry (1991) 30:3161-3169). Engel et al teach making a disulfide-bonded homodimer of a coiled-coil that binds to two copies of a cell-surface receptor, an integrin. Engel et al also teaches linking two different ligands to make a heterdimeric "RAMP" (receptor-adhesive modular protein). See entire document, especially pp. 3161-3162 and P164 in Figure 1. Integrins are believed to be signal transducers that result in gene transcription and extracellular matrix degradation (see for instance paragraph 0033 in Yacoby-Zeevi (US 2002/0088019).

14. Claims 1-3, 5 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Heidaran et al (J. Biol. Chem. (1991) 266:20323-20237). Heidaran et al teach making homodimers of PDGF-A or PDGF-B or heterodimers comprising PDGF-A and –B by

disulfide linkage. See entire document, especially p. 20232, Production of Recombinant PDGF-AB.

15. Claims 1-3 and 7 are rejected under 35 U.S.C. 102(e) as being anticipated by Kao et al (USP 5,120,727). Kao et al teach a method comprising covalently linking one rapamycin monomer to a second rapamycin monomer which has immunosuppressive, antifungal, antitumore and/or anti-inflammatory activity in vivo and inhibit thymocyte proliferation in vitro. See entire document.

Conclusion

Claims 1-7 are rejected.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from 10:00 AM to 6:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than the next business day after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, can be reached on (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to Tracey Johnson, Patent Analyst whose telephone number is (703) 305-2982.

Customer service for Tech Center 1600 may be reached at (703)-308-0198.

Bronwen M. Loeb, Ph.D.
Patent Examiner
Art Unit 1636

September 29, 2002

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600